Oxytetracycline Bath Marking Clinical Field Trials - INAD 9033

Year 2000 Annual Summary Report on the Use of Oxytetracycline Bath Marking in Field Efficacy Trials

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Summary

Oxytetracycline for bath marking was used at one U.S. Fish and Wildlife Service fish hatchery, and four state fish hatcheries during year 2000 to mark the otoliths of young fish. The U.S. Food and Drug Administration has authorized the use of this compound under Compassionate Investigational New Animal Drug Exemption #9033 for the purpose of collecting pivotal and ancillary efficacy data to support a new animal drug approval for oxytetracycline. Oxytetracycline for bath marking was administered in 15 trials and involved approximately 40.1 million fish. Eleven trials appeared efficacious as a readable mark was observed in a sub-sample of treated fish, and 4 trials were characterized as inconclusive as mark confirmation was not conducted on fish prior to release.

Introduction

Water soluble oxytetracycline is an effective and convenient marking agent for use on early life stages of fish. Large numbers of fish can be marked simultaneously by simple exposure to a uniform oxytetracycline solution for up to several hours. In many cases, immersion marking with oxytetracycline is the only practical means of permanently marking large numbers of small fish for the purpose of evaluating fishery management strategies. In general, marking is accomplished by immersing very young fish in a bath containing 500 mg/L oxytetracycline and 1000 mg/L sodium chloride, buffered with Tris buffer to a pH of 6.5 - 6.9, for six hours. Sodium chloride is necessary to prevent calcium chelation of the oxytetracycline.

The overall objective of these trials was to develop clinical field efficacy data on the use of water soluble oxytetracycline as an agent for the non-intrusive marking of fish larvae, fry, or very young fish prior to, or shortly after, initiation of feeding. Fish of such small size cannot be marked by fin clip or other more conventional tagging procedures. Fish marked at early life stages are not available for human consumption until they have grown to a much larger size, which in virtually all cases requires at least a year or more

of additional growth. Except for threatened and endangered species and research fish destroyed after use, no fish averaging larger than 2 grams each are authorized for oxytetracycline treatment under INAD 9033.

Purpose

The purpose of this report is to summarize the results of calendar year (CY 2000) supplemental oxytetracycline for bath marking (OXM) field efficacy studies. However, it is also expected that these data will be used to enhance the existing OXM database that has been established from previous years studies for the purpose of expanding and/or extending the approved label for oxytetracycline use in aquaculture.

Facilities, Materials, and Methods

1. Facilities

A total of 1 U.S. Fish and Wildlife Service fish hatchery, and 4 state fish hatcheries used OXM during CY 2000.

2. OXM used in trials

All OXM used in these trials was Terramycin-343 soluble powder supplied by Pfizer, Inc., Lee's Summit, Missouri. Pfizer's over-the-counter Terramycin-343 soluble powder contains 343 grams of active oxytetracycline hydrochloride per pound. Pfizer's Terramycin-343 was the only form of oxytetracycline used by fish culturists to treat fish under INAD #9033.

3. Drug dosages

As described in the Study Protocol for INAD #9033, oxytetracycline was administered as a single bath treatment for 6 hours at a dosage of 500 mg/L.

Fish Species

1. Species of fish treated

The only fish species treated during CY 2000 was the walleye (*Sitzostedion vitreum*).

2. Marking

Fish were treated with oxytetracycline to provide a mark that could be used as an important fishery management tool.

Data Collected

1. Pathologists Reports

Fish health pathology reports provide essential information with respect to disease confirmation and general fish health. However, no pathology reports were submitted during CY 2000 studies.

2. Efficacy of marking procedure

A sub-sample of fish were collected from the treated fish and evaluated for the presence of a mark by examination of the otoliths.

3. Mortality data

As stated in the Study Protocol, mortality data was to be collected for at least 10 days prior to treatment and for at least 30 d post-treatment. The Investigators noted that no mortalities were observed during or immediately after the treatment. However, some of the walleye were stocked out immediately after treatment.

Discussion of Study Results

1. **Summary results on the efficacy of OTC for marking fish** (Note: A summary of the state fish hatcheries individual OXM studies conducted during CY 2000 under INAD 9033 is presented in Table 3; and summary data regarding all studies conducted is presented in Table 1).

A. Efficacy of OXM at 500 mg/L

OXM was used in 15 trials involving walleye (Table 1). OXM treatment appeared efficacious in 11 trials as a "readable mark" was confirmed from a sub-sample of walleye collected after the OXM treatment. Four trials involving the walleye were characterized as inconclusive because no mark confirmation was conducted (fish were stocked out immediately after treatment). Investigators noted that the fish appeared to be in excellent condition after the treatment and no mortalities were observed.

2. Observed Toxicity

No toxicity or adverse effects relating to OXM treatment were reported.

Summary of Study Results

OXM was used as a single bath treatment for 6 hours at a dosage of 500 mg/L in 15 trials involving walleye. Approximately 40.1 million early life stage fish (fry) were treated. Water temperature during treatment ranged from 53 - 68°F. Approximately 73% of the trials appeared efficacious, while 27% were characterized as inconclusive. Furthermore, Investigators reported no evidence of toxicity or adverse effects related to OXM treatment in all trials. Although these data must be considered as ancillary efficacy data, they should provide useful corroborative data to support a future expanded label claim for oxytetracycline. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #9033. In future trials conducted under INAD #9033, efforts will be directed towards the generation of higher quality data.

Table 1. Summary of Year 2000 Oxytetracycline Bath Marking Efficacy Results

Hatchery	Number of Trials	Fish Species	Number of Fish	Treatment type	Treatment Duration (hrs)	Dose (mg/L)	pH	Dissolved Oxygen	Temp. (°F)
Bubbling Ponds Hatchery	1	WAE	80,000	Immersion	6	500	na	na	68.0
Garrison Dam NFH	10	WAE	12,755,000	Immersion	6	500	7.0 - 7.1	9 - 15	53.0 - 62.0
Miles City SFH	1	WAE	27,000,000	Immersion	6	500	na	na	54.0
Milford Fish Hatchery	2	WAE	215,258	Immersion	6	500	na	na	58.0 - 68.0
Table Rock SFH	1	WAE	30,000	Immersion	6	500	na	na	66.0

Table 2. Summary Data Regarding Year 2000 Oxytetracycline for Bath Marking Efficacy Studies

Total Number of Fish Treated:	40,080,258
Treatment Regimes Used:	
500 mg/L static bath for 6 hr	15 trials
Treatment Water Temperature (°F):	53.0 - 68.0
Size of Treated Fish:	Fry
Species Treated:	walleye (*Sitzostedion vitreum*)